

=> file hcaplus

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FILE COVERS 1907 - 1 Feb 2007 VOL 146 ISS 6
FILE LAST UPDATED: 31 Jan 2007 (20070131/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que nos l14

L13 25 SEA FILE=HCAPLUS ABB=ON PLU=ON SAVVA M?/AU
L14 10 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 AND LIPID?

=> file uspatfull

FILE 'USPATFULL' ENTERED AT 18:42:49 ON 01 FEB 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 1 Feb 2007 (20070201/PD)
FILE LAST UPDATED: 1 Feb 2007 (20070201/ED)
HIGHEST GRANTED PATENT NUMBER: US7171694
HIGHEST APPLICATION PUBLICATION NUMBER: US2007028338
CA INDEXING IS CURRENT THROUGH 1 Feb 2007 (20070201/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 1 Feb 2007 (20070201/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2006

=> d que nos l17

L13 25 SEA FILE=HCAPLUS ABB=ON PLU=ON SAVVA M?/AU
L17 2 SEA FILE=USPATFULL ABB=ON PLU=ON L13 AND LIPID?

=> file hcaplus uspatfull

FILE 'HCAPLUS' ENTERED AT 18:43:12 ON 01 FEB 2007
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FILE 'USPATFULL' ENTERED AT 18:43:12 ON 01 FEB 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

=> dup rem l14 l17

PROCESSING COMPLETED FOR L14
PROCESSING COMPLETED FOR L17

L19 10 DUP REM L14 L17 (2 DUPLICATES REMOVED)
ANSWERS '1-10' FROM FILE HCAPLUS

=> d ibib ed abs hitstr 1-10

10/686262

L19 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2005:394541 HCAPLUS Full-text
DOCUMENT NUMBER: 142:435781
TITLE: Single-component pH-sensitive liposomes of
reduced solid-to-liquid phase transition
temperatures for gene delivery
INVENTOR(S): Savva, Michalakis
PATENT ASSIGNEE(S): Michalakis Savva, USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	

US 2005095280	A1	20050505	US 2003-686374	200310 15
PRIORITY APPLN. INFO.:			US 2003-686374	200310 15

OTHER SOURCE(S): MARPAT 142:435781

ED Entered STN: 09 May 2005

AB The current invention relates to the synthesis of novel cationic lipids and their use as delivery vectors for nucleic acids, peptides and other synthetic drugs, in vitro and in vivo. The cationic lipids described herein form stable lamellar structures (liposomes) at physiol. pH but destabilize to micelles at acidic and alkaline pH. These structures are characterized by high elasticity, increased fluidity and high transfection activity relative to the corresponding 1,2-dialkyl cationic derivs. and other phospholipids analogs.

L19 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2005:346678 HCAPLUS Full-text
DOCUMENT NUMBER: 142:417187
TITLE: Cationic lipids for nucleic acid
delivery
INVENTOR(S): Savva, Michalakis
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	

US 2005084522	A1	20050421	US 2003-686262	200310 15
PRIORITY APPLN. INFO.:			US 2003-686262	200310 15

OTHER SOURCE(S): MARPAT 142:417187

ED Entered STN: 22 Apr 2005

AB The invention describes the synthetic methods for a series of pH-sensitive cationic lipids with diamido linkages between the 1,2-diamino-3-propanol backbone and the hydrocarbon chains. Their in vitro biol. activity of the resulting lipid-DNA complexes is also described.

L19 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1162755 HCAPLUS Full-text

DOCUMENT NUMBER: 144:74592

TITLE: In Vitro Lipofection with Novel Asymmetric Series of 1,2-Dialkoylamidopropane-Based Cytofectins Containing Single Symmetric Bis-(2-dimethylaminoethane) Polar Headgroups

AUTHOR(S): Savva, Michalakis; Chen, Pensung;

CORPORATE SOURCE: Aljaberi, Ahmad; Selvi, Bilge; Spelios, Michael
Division of Pharmaceutical Sciences, Arnold Marie Schwartz College of Pharmacy and Health Sciences, Long Island University, Brooklyn, NY, 11201, USASOURCE: Bioconjugate Chemistry (2005), 16(6), 1411-1422
CODEN: BCCHE; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 01 Nov 2005

AB Novel N,N'-diacyl-1,2-diaminopropyl-3-carbamoyl[bis-(2- dimethylaminoethane)] bivalent cationic lipids were synthesized and evaluated for in vitro transfection activity against a murine melanoma cell line. In the absence of the helper lipid DOPE (1,2-dioleoyl-sn-glycero-3-phosphoethanolamine), only the dioleoyl derivative 22 (1,2lb5) elicited transfection activity. The transfection activity of this lipid was reduced when formulated with DOPE. Contrary to that, the dimyristoyl derivative 19 (1,2lb2) mediated no activity when used alone but induced the highest levels of marker gene expression in the presence of DOPE. In an effort to correlate the transfection activity with cationic lipid structures, the physicochem. properties of cationic lipids in isolation and of lipoplexes were studied with surface tensiometry, photon correlation spectroscopy, gel electrophoresis mobility shift assay, and fluorescence techniques. In regard to the lipoplex properties, gel electrophoresis mobility shift assay and EtBr exclusion fluorescence assay revealed that the 1,2lb5 was the only lipid to associate and condense plasmid DNA, resp. Photon correlation spectroscopy anal. found that 1,2lb5/DNA complexes were of relatively small size compared to all other lipoplexes. With respect to the properties of isolated lipids, Langmuir monolayer studies and fluorescence anisotropy on cationic lipid dispersions verified high two-plane elasticity and increased fluidity of the transfection competent dioleoyl derivative 1,2lb5, resp. The results indicate that high transfection activity is mediated by cationic lipids characterized by an expanded mean mol. area, high mol. elasticity, and increased fluidity.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L19 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:25928 HCAPLUS Full-text

DOCUMENT NUMBER: 143:272152

TITLE: Synthesis, in vitro transfection activity and physicochemical characterization of novel N,N'-diacyl-1,2-diaminopropyl-3-carbamoyl-(dimethylaminoethane) amphiphilic derivatives

AUTHOR(S): Aljaberi, Ahmad; Chen, Pensung; Savva, Michalakis

CORPORATE SOURCE: Division of Pharmaceutical Sciences, Arnold and Marie Schwartz College of Pharmacy and Health Sciences, Long Island University, Brooklyn, NY, 11201, USA

SOURCE: Chemistry and Physics of Lipids (2005), 133(2), 135-149
CODEN: CPLIA4; ISSN: 0009-3084

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 12 Jan 2005

AB A novel series of N,N'-diacyl-1,2-diaminopropyl-3-carbamoyl- (dimethylaminoethane) cationic derivs. was synthesized and screened for in vitro transfection activity at

different charge ratios in the presence and absence of the helper lipids DOPE and cholesterol. Physicochem. properties of lipid-DNA complexes were studied by gel electrophoresis, fluorescence spectroscopy and dynamic light scattering. The interfacial properties of the lipids in isolation were studied using the Langmuir film balance technique at 23 °C. It was found that only lipoplexes formulated with the dioleoyl derivative, 1,2lmt[5], mediated significant in vitro transfection activity. Optimum activity was obtained with 1,2lmt[5]/DOPE mixture at a \pm charge ratio of 2. In agreement with the transfection results, 1,2lmt[5] was the only lipid found to complex and retard DNA migration as verified by gel electrophoresis. Despite the efficient complexation, no significant condensation of plasmid DNA was observed as indicated by fluorescence spectroscopy measurements. Monolayer studies showed that the dioleoyl derivative 1,2lmt[5] was the only lipid that existed in an all liquid-expanded state with a collapse area and collapse pressure of 59.5 Å² and 38.7 mN/m, resp. This lipid was also found to have the highest elasticity with a compressibility modulus at monolayer collapse of 80.4 mN/m. In conclusion, increased acyl chain fluidity and high mol. elasticity of cationic lipids were found to correlate with improved transfection activity.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L19 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:503242 HCAPLUS Full-text

DOCUMENT NUMBER: 144:198343

TITLE: Correlation of the physicochemical properties of
symmetric 1,3-dialkoylamidopropane-based
cationic lipids containing single
primary and tertiary amine polar head groups
with in vitro transfection activity

AUTHOR(S): Savva, Michalakis; Aljaberi, Ahmad;
Feig, Jennifer; Stolz, Donna Beer

CORPORATE SOURCE: Division of Pharmaceutical Sciences, Arnold and
Marie Schwartz College of Pharmacy and Health
Sciences, Long Island University, Brooklyn, NY,
11201, USA

SOURCE: Colloids and Surfaces, B: Biointerfaces (2005),
43(1), 43-56
CODEN: CSBBEQ; ISSN: 0927-7765

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 13 Jun 2005

AB The physicochem. properties of a novel series of sym. 1,3-dialkylamidopropane-based cationic amphiphiles [M. Sheikh, J. Feig, B. Gee, S. Li, M. Savva, In vitro lipofection with novel series of sym. 1,3-dialkoylamidopropane-based cationic surfactants containing single primary and tertiary amine polar head groups, Chemical Phys. Lipids 124 (2003) 49-61] were studied by several techniques, in an effort to correlate cationic lipid structure with transfection efficacy. It was found that only the unsubstituted amine and tertiary amine dioleoyl derivs. 1,3lmp5 and 1,3lmt5, resp., mediated in vitro transfection activity in the absence of helper lipids. This activity pattern was consistent with ethidium bromide fluorescence quenching studies, which indicated that only these two derivs. bound to and efficiently condense plasmid DNA at physiol. pH. Dynamic light scattering indicated that lipoplexes made by these two cationic lipids were relatively small particles below 1 µm, in sharp contrast to lipoplexes bigger than 3 µm composed of saturated cationic derivs. Transmission electron microscopy studies clearly indicated that cationic lipid dispersions made by saturated derivs. form multilamellar tubules at physiol. pH. Calorimetric studies showed that cationic amphiphiles with saturated acyl chains longer than 12 carbons exhibit solid-to-liquid crystalline phase transitions above 37 °C. In agreement with the microscopy and calorimetry studies, Langmuir film balance expts. indicated that saturated derivs. with hydrophobic chains longer than 12 carbons are not well hydrated and exist at a chain-ordered state at ambient temperature. Calcn. of compressibility moduli from monolayer compression isotherms at 23 °C suggested that monolayers made by cationic lipids bearing saturated acyl chains are less compressible relative to those of the dioleoyl derivs. 1,3lmp5 and 1,3lmt5. In conclusion, high hydration, increased

fluidity and high elasticity of cationic lipid assemblies in isolation, all correlate with high in vitro transfection activity.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L19 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:423359 HCAPLUS Full-text

DOCUMENT NUMBER: 140:88218

TITLE: In vitro lipofection with novel series of
symmetric 1,3-dialkoylamidopropane-based
cationic surfactants containing single primary
and tertiary amine polar head groups

AUTHOR(S): Sheikh, Mohammad; Feig, Jennifer; Gee, Becky;
Li, Song; Savva, Michalakis

CORPORATE SOURCE: Arnold & Marie Schwartz College of Pharmacy and
Health Sciences, Division of Pharmaceutics, Long
Island University, Brooklyn, NY, 11201, USA

SOURCE: Chemistry and Physics of Lipids (2003), 124(1),
49-61

CODEN: CPLIA4; ISSN: 0009-3084

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 03 Jun 2003

AB A novel series of sym. double-chained primary and tertiary 1,3-dialkoylamido monovalent cationic lipids were synthesized and evaluated for their transfection activities. In the absence of the helper lipid DOPE (1,2-dioleoyl-sn-glycero-3-phosphoethanolamine), only the primary and tertiary dioleoyl derivs. 1,3lmp5 and 1,3lmt5, resp. elicited transfection activity. This is a striking difference between sym. 1,2-diacyl glycerol-based monovalent cationic lipids that always found both dioleoyl and dimyristoyl analogs being efficient transfection reagents. In the presence of helper lipid, all cationic derivs. induced marker gene expression, except the dilauroyl analogs 1,3lmp1 and 1,3lmt1 that elicited no transfection activity. Combining electrophoretic mobility data of the lipoplexes at different charge ratios with transfection activity suggested two requirements for high transfection activity with monovalent double-chained cationic lipids, i.e., binding/association of the lipid to the plasmid DNA and membrane fusion properties of the lipid layers surrounding the DNA.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L19 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:647605 HCAPLUS Full-text

DOCUMENT NUMBER: 132:46579

TITLE: Effect of PEG homopolymer and grafted
amphiphilic PEG-palmityl on the thermotropic
phase behavior of 1,2-dipalmitoyl-sn-glycero-3-
phosphocholine bilayer

AUTHOR(S): Savva, Michalakis; Huang, Leaf

CORPORATE SOURCE: Departments of Pharmaceutical Sciences and
Pharmacology, University of Pittsburgh,
Pittsburgh, PA, 15261, USA

SOURCE: Journal of Liposome Research (1999), 9(3),
357-365

CODEN: JLREE7; ISSN: 0898-2104

PUBLISHER: Marcel Dekker, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 12 Oct 1999

AB Phospholipids covalently attached to polyethylene glycol (PEG-PE) are routinely used for the preparation of long-circulating liposomes. The common preparation procedure for long-circulating liposomes involves use of organic solvent. Although there is a plethora of studies describing the interaction of PEG-PE with bilayers, little is known about the effects of PEG homopolymers and single chain amphiphilic PEG on liposome structure. In the present investigation the interaction of PEG homopolymer and amphiphilic PEG-palmityl conjugate with large multilamellar liposomes composed of 1,2-

dipalmitoyl-sn-glycero-phosphocholine was investigated utilizing differential scanning calorimetry. Vesicle and aggregate sizes were determined by dynamic light scattering. DSC thermograms revealed interaction of PEG homopolymer with DPPC when the two are premixed in organic solvent. The data suggest that PEG interacts with the phospholipid acyl chains deep in the bilayer. Several questions are raised regarding the suitability of the current procedure for preparation of long-circulating liposomes which utilizes organic solvent. Incorporation of only 2 mol% 5 kDa PEG-palmityl conjugate completely solubilized DPPC liposomes. Packing geometry of the lipid anchor, irrespectively of the polymer molecular weight, is suggested to be the primary factor for successful grafting of hydrophilic polymers on liposomes. Pure PEG-palmityl formed self-assembled organized structures of potential use in the delivery of poorly soluble drugs.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L19 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:502263 HCAPLUS Full-text

DOCUMENT NUMBER: 131:327399

TITLE: Effect of Grafted Amphiphilic PVP-Palmityl
Polymers on the Thermotropic Phase Behavior of
1,2 Dipalmitoyl-sn-glycero-3-phosphocholine
Bilayer

AUTHOR(S): Savva, Michalakis; Torchilin, Vladimir
P.; Huang, Leaf

CORPORATE SOURCE: Departments of Pharmaceutical Sciences and
Pharmacology, University of Pittsburgh,
Pittsburgh, PA, 15261, USA

SOURCE: Journal of Colloid and Interface Science (1999),
217(1), 166-171
CODEN: JCISA5; ISSN: 0021-9797

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 12 Aug 1999

AB To better understand how grafted polymers interact with liposome membrane, a comparative study was conducted to investigate the influence of different chain length polyvinyl pyrrolidone-palmityl (PVP-p) conjugates on the thermotropic phase behavior of 1,2 dipalmitoyl-sn-glycero-3-phosphatidylcholine (DPPC) bilayer. Lipid-polymer dispersions were prepared by mixing DPPC and variable concns. of PVP-p conjugates in chloroform. Hydration of lipids was performed at 50-55°C after complete elimination of the organic solvent. DSC was used to determine lipid miscibility and bilayer-polymer interactions. Particle size was determined by photon correlation spectroscopy. Increasing concns. of 6 kDa PVP-p caused a shift of the main phase transition of DPPC at lower temps. At 9.1 mol% the DPPC phase pretransition (Tp) is abolished. At 16.7 mol%, differential scanning calorimetry showed an endothermic phase transition at 24.9°C. The enthalpy of this transition was twice as high compared to the main phase transition enthalpy of pure DPPC. Inclusion of more than 20 mol% of 6 kDa PVP-p resulted in a complete bilayer micellization. Qual. similar to the 6 kDa were the results obtained with the 12 kDa PVP-p conjugate. Increasing concns. of 25 kDa PVP-p from 1 to 13 mol% resulted in a decrease of the main DPPC phase transition temperature. At 13 mol% the new mol. self-assembled structure as previously identified with the lower MW PVP-p conjugates also showed up at the DSC thermogram. However, in sharp contrast to the lower MW PVP-p conjugates, increasing the 25 kDa PVP-p content did not result in bilayer disruption; rather, it resulted in a bilayer stabilization. The consequences of the hydrophobically modified PVP interaction with the bilayer are considered neg. with respect to the long-circulating properties of liposomes in the blood. (c) 1999 Academic Press.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L19 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:502262 HCAPLUS Full-text

DOCUMENT NUMBER: 131:327398

TITLE: Effect of Polyvinylpyrrolidone on the Thermal
Phase Transition of 1,2-Dipalmitoyl-sn-glycero-3-

phosphocholine Bilayer
 AUTHOR(S): Savva, Michalakis; Torchilin, Vladimir
 P.; Huang, Leaf
 CORPORATE SOURCE: Departments of Pharmaceutical Sciences and
 Pharmacology, University of Pittsburgh,
 Pittsburgh, PA, 15261, USA
 SOURCE: Journal of Colloid and Interface Science (1999),
 217(1), 160-165
 CODEN: JCISA5; ISSN: 0021-9797
 PUBLISHER: Academic Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 12 Aug 1999

AB The purpose of this study was to investigate the interaction of polyvinyl pyrrolidone (PVP) with phospholipid bilayers in an effort to add a new dimension to our understanding of polymer interaction with lipids. For the preparation of lipid-polymer dispersions, measured amts. of DPPC (1,2 dipalmitoyl-sn-glycero-3- phosphocholine) and PVP were mixed in chloroform. After complete elimination of organic solvent, the dry mixts. were hydrated at 50-55°C. Interactions between DPPC and PVP were assessed by DSC and photon correlation spectroscopy (PS). Separation of liposomes and micelles was performed by centrifugation. Liquid scintillation counting and a UV spectrophotometer were used for their anal. PVP added as dry powder or added as aqueous solution to dry lipid or preformed liposomes failed to interact. Only PVP previously dissolved in chloroform interacted with DPPC. The DPPC main phase transition moved to lower temps. with increasing PVP concns. This reduction of the phase transition temperature was accompanied by an increase of the DPPC phase transition enthalpy. Anal. of solubilization indicated that the amount of PVP present in the bilayer is dependent on the PVP bulk concentration. The data suggest interaction of PVP previously dissolved in chloroform with the acyl chains of the phospholipid deep into the bilayer. (c) 1999 Academic Press.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE
 IN THE RE FORMAT

L19 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:481727 HCAPLUS Full-text
 DOCUMENT NUMBER: 129:235495
 TITLE: PVP: a "pretender" molecule
 AUTHOR(S): Savva, M.; Torchilin, V. P.; Huang, L.
 CORPORATE SOURCE: University of Pittsburgh, Pittsburgh, PA, 15261,
 USA
 SOURCE: Proceedings of the International Symposium on
 Controlled Release of Bioactive Materials
 (1998), 25th, 134-135
 CODEN: PCRMEY; ISSN: 1022-0178
 PUBLISHER: Controlled Release Society, Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 04 Aug 1998

AB It appears that dipalmitoylphosphatidylcholine-PVP prepns. are stabilized through an enthalpic contribution. The observed lipid-polymer interaction is attributed to a change in the conformation of PVP, taking place during its dissoln. in organic solvent. Thus, PVP is a pretender mol. being able to acquire an appropriate conformation in a given environment. This can be of significant importance in formulations in which apolar solvents are used, e.g., transdermal and other topical dosage forms. In these formulations, the polymer might be presented in a hydrophobic conformation, thereby promoting keratinocyte barrier fluidization or interaction with living cells and other tissue components.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR
 THIS RECORD. ALL CITATIONS AVAILABLE IN
 THE RE FORMAT

=> d his nofile

(FILE 'HOME' ENTERED AT 17:39:02 ON 01 FEB 2007)

FILE 'REGISTRY' ENTERED AT 18:36:49 ON 01 FEB 2007
 ACT KIS374B/A

 L1 STR
 L2 SCR 1950 AND 1994
 L3 SCR 1363 OR 1236
 L4 SCR 1838
 L5 (3307)SEA SSS FUL L1 AND L2 AND L3 NOT L4
 L6 STR
 L7 14 SEA SUB=L5 SSS FUL L6

FILE 'HCAPLUS' ENTERED AT 18:37:12 ON 01 FEB 2007
 E US20050084522/PN

L8 1 SEA ABB=ON PLU=ON US2005084522/PN
 SEL RN

FILE 'REGISTRY' ENTERED AT 18:37:44 ON 01 FEB 2007

L9 30 SEA ABB=ON PLU=ON (108861-05-8/BI OR 108861-06-9/BI OR
 163333-56-0/BI OR 170515-15-8/BI OR 192223-81-7/BI OR
 54897-59-5/BI OR 6059-44-5/BI OR 850254-71-6/BI OR
 850254-72-7/BI OR 850254-73-8/BI OR 850254-74-9/BI OR
 850254-75-0/BI OR 850254-76-1/BI OR 850254-77-2/BI OR
 850254-78-3/BI OR 850254-79-4/BI OR 850254-80-7/BI OR
 850254-81-8/BI OR 850254-82-9/BI OR 850254-83-0/BI OR
 850254-84-1/BI OR 850254-85-2/BI OR 850254-86-3/BI OR
 850254-87-4/BI OR 850254-88-5/BI OR 850254-89-6/BI OR
 850254-90-9/BI OR 850254-91-0/BI OR 850254-92-1/BI OR
 850254-93-2/BI)

FILE 'HCAPLUS' ENTERED AT 18:37:54 ON 01 FEB 2007

L10 1 SEA ABB=ON PLU=ON L8 AND L9

FILE 'REGISTRY' ENTERED AT 18:38:05 ON 01 FEB 2007

L11 13 SEA ABB=ON PLU=ON L9 AND L7

FILE 'HCAPLUS' ENTERED AT 18:38:23 ON 01 FEB 2007

L12 3 SEA ABB=ON PLU=ON L7
 L13 25 SEA ABB=ON PLU=ON SAVVA M?/AU
 L14 10 SEA ABB=ON PLU=ON L13 AND LIPID?
 L15 0 SEA ABB=ON PLU=ON L12 NOT L14

FILE 'USPATFULL' ENTERED AT 18:39:51 ON 01 FEB 2007

L16 1 SEA ABB=ON PLU=ON L7
 L17 2 SEA ABB=ON PLU=ON L13 AND LIPID?
 L18 0 SEA ABB=ON PLU=ON L16 NOT L17

FILE 'HCAPLUS' ENTERED AT 18:42:37 ON 01 FEB 2007
 D QUE NOS L14

FILE 'USPATFULL' ENTERED AT 18:42:49 ON 01 FEB 2007
 D QUE NOS L17

FILE 'HCAPLUS, USPATFULL' ENTERED AT 18:43:12 ON 01 FEB 2007

L19 10 DUP REM L14 L17 (2 DUPLICATES REMOVED)
 ANSWERS '1-10' FROM FILE HCAPLUS
 D IBIB ED ABS HITSTR 1-10

FILE 'REGISTRY' ENTERED AT 18:45:32 ON 01 FEB 2007
 D QUE STAT L7

FILE 'HCAPLUS' ENTERED AT 18:47:00 ON 01 FEB 2007

=> file reg

FILE 'REGISTRY' ENTERED AT 18:45:32 ON 01 FEB 2007

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DICTIONARY FILE UPDATES: 31 JAN 2007 HIGHEST RN 918932-71-5

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TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

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=> d que stat 17

L1 STR

N~Ak~N Ak 4 Ak 5
1 2 3

NODE ATTRIBUTES:

CONNECT IS E2 RC AT 2

DEFAULT MLEVEL IS ATOM

MLEVEL IS CLASS AT 2 4 5

GGCAT IS SAT AT 2

DEFAULT ECLEVEL IS LIMITED

ECOUNT IS M11 C AT 4

ECOUNT IS M11 C AT 5

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 5

STEREO ATTRIBUTES: NONE

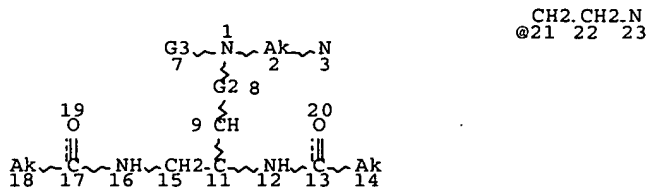
L2 SCR 1950 AND 1994

L3 SCR 1363 OR 1236

L4 SCR 1838

L5 (3307)SEA FILE=REGISTRY SSS FUL L1 AND L2 AND L3 NOT L4

L6 STR



REP G2=(1-4) A
VAR G3=H/CH3/21

NODE ATTRIBUTES:

CONNECT IS E2 RC AT 2
 DEFAULT MLEVEL IS ATOM
 MLEVEL IS CLASS AT 2 14 18
 DEFAULT ECLEVEL IS LIMITED
 ECOUNT IS M11 C AT 14
 ECOUNT IS M11 C AT 18

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

L7 14 SEA FILE=REGISTRY SUB=L5 SSS FUL L6

100.0% PROCESSED 366 ITERATIONS

14 ANSWERS

SEARCH TIME: 00.00.01

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FILE 'HCAPLUS' ENTERED AT 18:47:00 ON 01 FEB 2007

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FILE COVERS 1907 - 1 Feb 2007 VOL 146 ISS 6

FILE LAST UPDATED: 31 Jan 2007 (20070131/ED)

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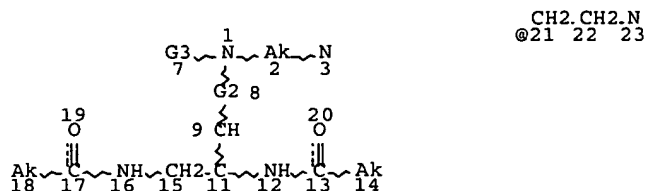
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10/686262

L2 SCR 1950 AND 1994
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L4 SCR 1838
L5 (3307)SEA FILE=REGISTRY SSS FUL L1 AND L2 AND L3 NOT L4
L6 STR



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FILE 'USPATFULL' ENTERED AT 18:48:23 ON 01 FEB 2007
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 1 Feb 2007 (20070201/PD)
FILE LAST UPDATED: 1 Feb 2007 (20070201/ED)
HIGHEST GRANTED PATENT NUMBER: US7171694
HIGHEST APPLICATION PUBLICATION NUMBER: US2007028338
CA INDEXING IS CURRENT THROUGH 1 Feb 2007 (20070201/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 1 Feb 2007 (20070201/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2006

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L4 SCR 1838
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L20 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2005:346678 HCAPLUS Full-text
DOCUMENT NUMBER: 142:417187
TITLE: Cationic lipids for nucleic acid delivery
INVENTOR(S): Savva, Michalakakis
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2005084522	A1	20050421	US 2003-686262	20031015
RITY APPLN. INFO.:			US 2003-686262	20031015

OTHER SOURCE(S) : MARPAT 142:417187

ED Entered STN: 22 Apr 2005

AB The invention describes the synthetic methods for a series of pH-sensitive cationic lipids with diamido linkages between the 1,2-diamino-3-propanol backbone and the hydrocarbon chains. Their in vitro biol. activity of the resulting lipid-DNA complexes is also described.

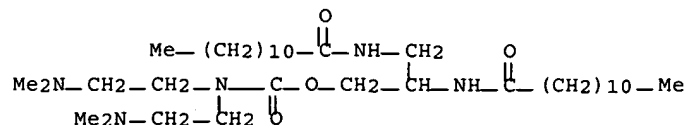
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	850254-93-2P		

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(cationic lipids for nuclei acid delivery)

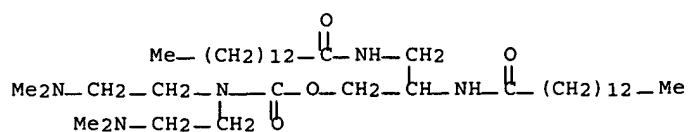
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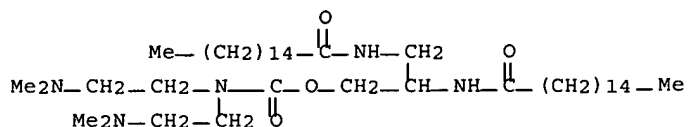
RN 850254-82-9 HCAPLUS

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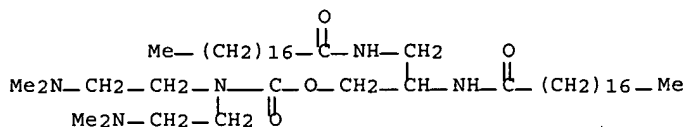
RN 850254-83-0 HCAPLUS

CN Carbamic acid, bis[2-(dimethylamino)ethyl]-, 2,3-bis[(1-oxohexadecyl)amino]propyl ester (9CI) (CA INDEX NAME)



RN 850254-84-1 HCAPLUS

CN Carbamic acid, bis[2-(dimethylamino)ethyl]-, 2,3-bis[(1-oxooctadecyl)amino]propyl ester (9CI) (CA INDEX NAME)

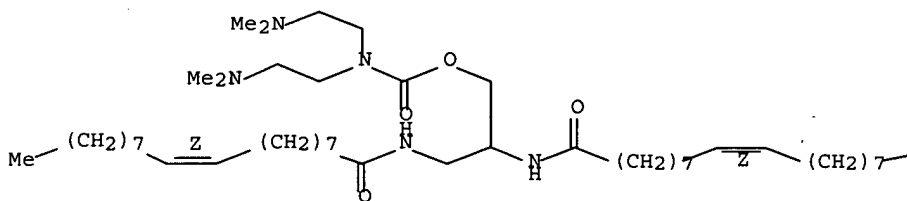


RN 850254-85-2 HCAPLUS

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Double bond geometry as shown.

PAGE 1-A



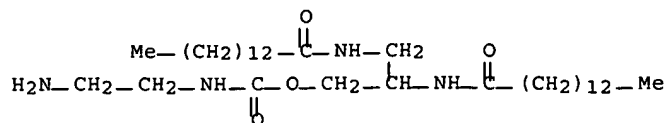
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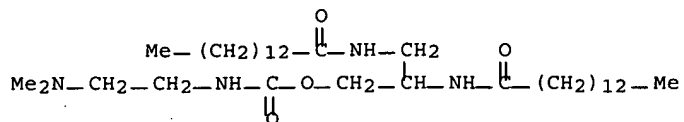
10/686262

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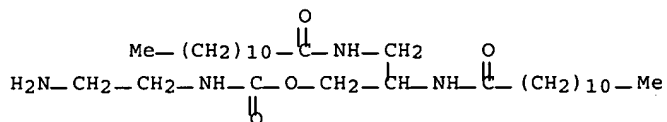
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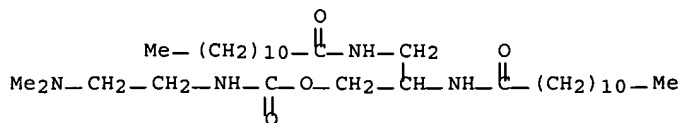
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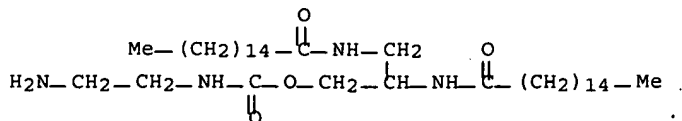
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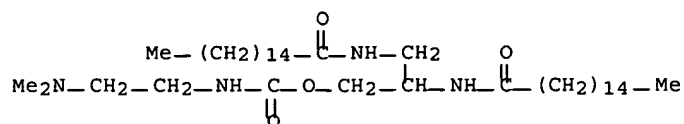


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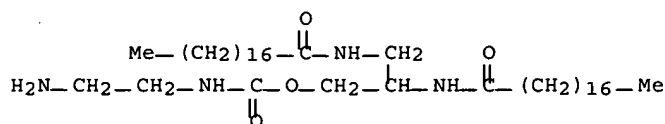
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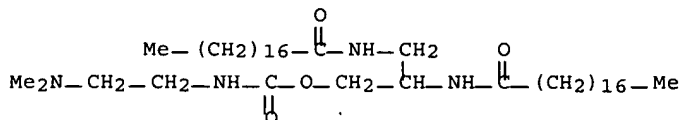
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RN 850254-92-1 HCAPLUS
 CN Carbamic acid, (2-aminoethyl)-, 2,3-bis[(1-oxooctadecyl)amino]propyl ester (9CI) (CA INDEX NAME)



RN 850254-93-2 HCAPLUS
 CN Carbamic acid, [2-(dimethylamino)ethyl]-, 2,3-bis[(1-oxooctadecyl)amino]propyl ester (9CI) (CA INDEX NAME)



L20 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1162755 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 144:74592

TITLE: In Vitro Lipofection with Novel Asymmetric Series of 1,2-Dialkoylamidopropane-Based Cytofectins Containing Single Symmetric Bis-(2-dimethylaminoethane) Polar Headgroups

AUTHOR(S): Savva, Michalakis; Chen, Pensung; Aljaberi, Ahmad; Selvi, Bilge; Spelios, Michael

CORPORATE SOURCE: Division of Pharmaceutical Sciences, Arnold Marie Schwartz College of Pharmacy and Health Sciences, Long Island University, Brooklyn, NY, 11201, USA

SOURCE: Bioconjugate Chemistry (2005), 16(6), 1411-1422
 CODEN: BCCHE; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 01 Nov 2005

AB Novel N,N'-diacyl-1,2-diaminopropyl-3-carbamoyl[bis-(2-dimethylaminoethane)] bivalent cationic lipids were synthesized and evaluated for in vitro transfection activity against a murine melanoma cell line. In the absence of the helper lipid DOPE (1,2-dioleoyl-sn-glycero-3-phosphoethanolamine), only the dioleoyl derivative 22 (1,2lb5) elicited transfection activity. The transfection activity of this lipid was reduced

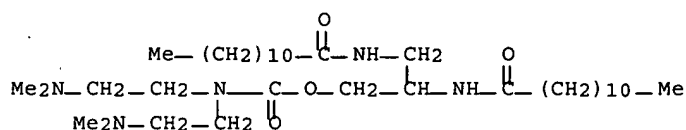
when formulated with DOPE. Contrary to that, the dimyristoyl derivative 19 (1,2lb2) mediated no activity when used alone but induced the highest levels of marker gene expression in the presence of DOPE. In an effort to correlate the transfection activity with cationic lipid structures, the physicochem. properties of cationic lipids in isolation and of lipoplexes were studied with surface tensiometry, photon correlation spectroscopy, gel electrophoresis mobility shift assay, and fluorescence techniques. In regard to the lipoplex properties, gel electrophoresis mobility shift assay and EtBr exclusion fluorescence assay revealed that the 1,2lb5 was the only lipid to associate and condense plasmid DNA, resp. Photon correlation spectroscopy anal. found that 1,2lb5/DNA complexes were of relatively small size compared to all other lipoplexes. With respect to the properties of isolated lipids, Langmuir monolayer studies and fluorescence anisotropy on cationic lipid dispersions verified high two-plane elasticity and increased fluidity of the transfection competent dioleoyl derivative 1,2lb5, resp. The results indicate that high transfection activity is mediated by cationic lipids characterized by an expanded mean mol. area, high mol. elasticity, and increased fluidity.

IT 850254-81-8P 850254-82-9P 850254-83-0P
850254-84-1P 850254-85-2P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (in vitro lipofection with novel asym. series of
 1,2-dialkoylamidopropane-based cytofectins containing single sym.
 bis-(2-dimethylaminoethane) polar headgroups)

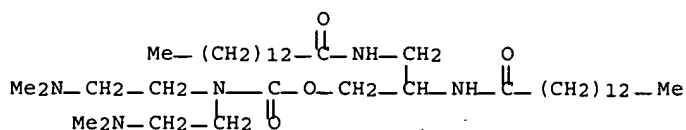
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CN Carbamic acid, bis[2-(dimethylamino)ethyl]-, 2,3-bis[(1-oxododecyl)amino]propyl ester (9CI) (CA INDEX NAME)



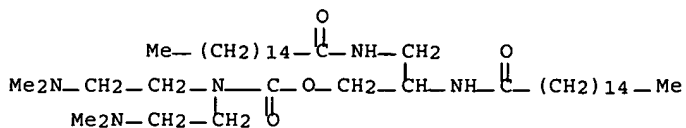
RN 850254-82-9 HCAPLUS

CN Carbamic acid, bis[2-(dimethylamino)ethyl]-, 2,3-bis[(1-oxotetradecyl)amino]propyl ester (9CI) (CA INDEX NAME)



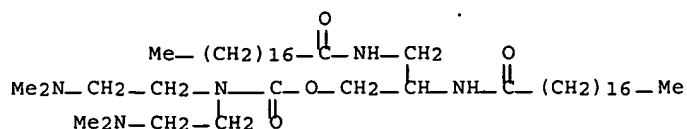
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CN Carbamic acid, bis[2-(dimethylamino)ethyl]-, 2,3-bis[(1-oxohexadecyl)amino]propyl ester (9CI) (CA INDEX NAME)



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CN Carbamic acid, bis[2-(dimethylamino)ethyl]-, 2,3-bis[(1-oxooctadecyl)amino]propyl ester (9CI) (CA INDEX NAME)

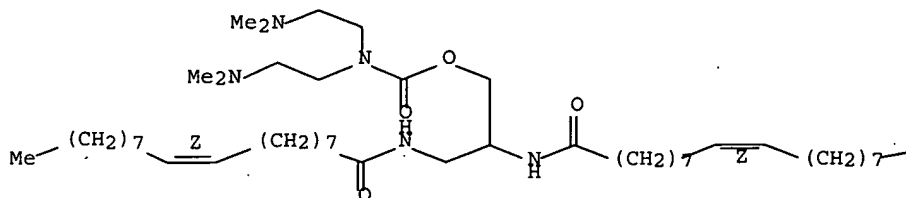


RN 850254-85-2 HCAPLUS

CN Carbamic acid, bis[2-(dimethylamino)ethyl]-, 2,3-bis[[(9Z)-1-oxo-9-octadecenyl]amino]propyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:25928 HCAPLUS Full-text

DOCUMENT NUMBER: 143:272152

TITLE: Synthesis, in vitro transfection activity and physicochemical characterization of novel N,N'-diacyl-1,2-diaminopropyl-3-carbamoyl-(dimethylaminoethane) amphiphilic derivatives

AUTHOR(S): Aljaberi, Ahmad; Chen, Pensung; Savva, Michalakos

CORPORATE SOURCE: Division of Pharmaceutical Sciences, Arnold and Marie Schwartz College of Pharmacy and Health Sciences, Long Island University, Brooklyn, NY, 11201, USA

SOURCE: Chemistry and Physics of Lipids (2005), 133(2), 135-149

CODEN: CPLIA4; ISSN: 0009-3084

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 12 Jan 2005

AB A novel series of N,N'-diacyl-1,2-diaminopropyl-3-carbamoyl- (dimethylaminoethane) cationic derivs. was synthesized and screened for in vitro transfection activity at

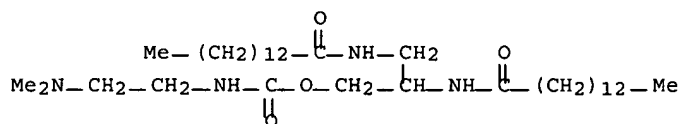
different charge ratios in the presence and absence of the helper lipids DOPE and cholesterol. Physicochem. properties of lipid-DNA complexes were studied by gel electrophoresis, fluorescence spectroscopy and dynamic light scattering. The interfacial properties of the lipids in isolation were studied using the Langmuir film balance technique at 23 °C. It was found that only lipoplexes formulated with the dioleoyl derivative, 1,2lmt[5], mediated significant in vitro transfection activity. Optimum activity was obtained with 1,2lmt[5]/DOPE mixture at a \pm charge ratio of 2. In agreement with the transfection results, 1,2lmt[5] was the only lipid found to complex and retard DNA migration as verified by gel electrophoresis. Despite the efficient complexation, no significant condensation of plasmid DNA was observed as indicated by fluorescence spectroscopy measurements. Monolayer studies showed that the dioleoyl derivative 1,2lmt[5] was the only lipid that existed in an all liquid-expanded state with a collapse area and collapse pressure of 59.5 Å² and 38.7 mN/m, resp. This lipid was also found to have the highest elasticity with a compressibility modulus at monolayer collapse of 80.4 mN/m. In conclusion, increased acyl chain fluidity and high mol. elasticity of cationic lipids were found to correlate with improved transfection activity.

IT 850254-87-4P 850254-89-6P 850254-91-0P
850254-93-2P 863581-97-9P

RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (preparation, in vitro transfection activity and physicochem. characterization of N,N'-diacyl-1,2-diaminopropyl-3-carbamoyl-(dimethylaminoethane) amphiphilic derivs.)

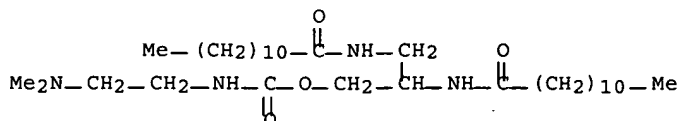
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CN Carbamic acid, [2-(dimethylamino)ethyl]-, 2,3-bis[(1-oxotetradecyl)amino]propyl ester (9CI) (CA INDEX NAME)



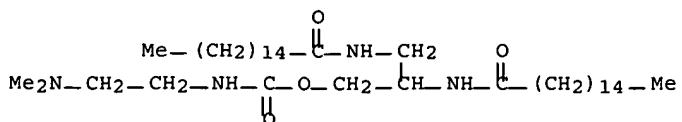
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CN Carbamic acid, [2-(dimethylamino)ethyl]-, 2,3-bis[(1-oxododecyl)amino]propyl ester (9CI) (CA INDEX NAME)



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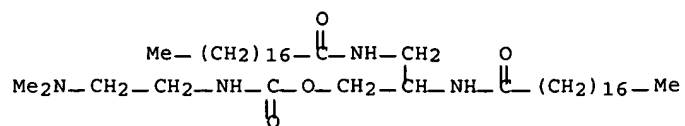


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10/686262

oxooctadecyl)amino]propyl ester (9CI) (CA INDEX NAME)

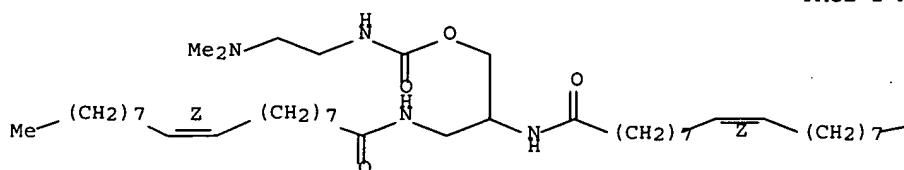


RN 863581-97-9 HCAPLUS

CN Carbamic acid, [2-(dimethylamino)ethyl]-, 2,3-bis[[[(9Z)-1-oxo-9-octadecenyl]amino]propyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

REFERENCE COUNT:

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THERE ARE 26 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

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